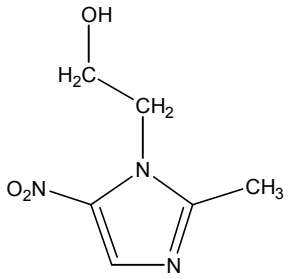
METRONIDAZOLE
CAS No. 443-48-1
First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

Metronidazole is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.13, 1977; IARC S.4, 1982; IARC S.7, 1987). When administered orally, metronidazole induced an increased incidence of lung tumors in mice of both sexes and lymphomas in female mice. Oral administration of the compound also caused mammary fibroadenomas and adenocarcinomas in female rats and pituitary, testicular, and liver tumors in rats.

There is inadequate evidence for the carcinogenicity of metronidazole in humans (IARC S.4, 1982; IARC S.7, 1987). Two epidemiological studies of women treated with metronidazole showed an excess of uterine cervix cancers, a neoplasm that has risk factors in common with vaginal trichomoniasis (for which metronidazole is administered). In one study, a greater excess of cervical cancer was observed in women with trichomoniasis who were not exposed to metronidazole. One of the two epidemiological studies showed an excess of lung cancer.

PROPERTIES

Metronidazole occurs as white to pale-yellow crystalline powder that is readily soluble in water. It is also soluble in ethanol, ether, chloroform, and dilute acids, and sparingly soluble in dimethylformamide. When heated to decomposition, metronidazole emits toxic fumes of nitrogen oxides (NO_x).

USE

Metronidazole is used primarily as a drug for the treatment of infections due to *Entamoeba histolytica*, *Trichomonas vaginalis*, and *Giardia lamblia*. Metronidazole has also been used to treat Vincent′s infection. It is prescribed for invasive intestinal amoebiasis or amoebic hepatic abscess. Metronidazole can also be used as a trichomonacide in veterinary medicine (IARC V.13, 1977). One firm petitioned EPA to use metronidazole as a disinfectant for cooling tower water.

PRODUCTION

Current production data were not available and no information on imports or exports was reported. Metronidazole was not listed in the 1979 TSCA Inventory. In 1976, total United States sales for metronidazole for use in human medicine was estimated to be < 28,000 lb (IARC V.13, 1977). In 1974, the USITC reported one firm producing metronidazole in the United States (USITC, 1975). Commercial production of metronidazole in the United States was first reported in 1961 (IARC V.13, 1977).

EXPOSURE

The primary routes of potential human exposure to metronidazole are ingestion of the drug for treatment of certain infectious diseases, dermal contact, and inhalation. A recommended oral dose regime is 750 mg three times per day for 5-10 days. As a systemic trichomonacidal agent, metronidazole is usually administered in a dose regime of 250 mg orally three times per day for 7 days. When used to treat giardiasis, metronidazole is administered in a daily dose of 500 mg for 5 days and repeated if necessary. Metronidazole has also been applied in pessaries in a dose of 500 mg daily for 10-20 days, indicating that a small population of women potentially experience vaginal or uterine exposure to the compound (IARC V.13, 1977). Potential occupational exposure may occur through inhalation and dermal contact for workers involved in the manufacture, formulation, packaging, or administration of metronidazole.

REGULATIONS

EPA regulates metronidazole under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as a microbicide/algicide for cooling tower water. FDA regulates metronidazole as a drug approved for human use. FDA also requires metronidazole to carry warning labels regarding its potential carcinogenicity, mutagenicity, teratogenicity, and/or impairment of fertility. OSHA regulates metronidazole under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-85.